

86	4462	elam\$ or ICAM\$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:07
92	0	(angiogen\$ ADJ factor) same fusion same (elam\$ or ICAM\$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:08
98	0	(angiogen\$ ADJ factor) same fusion same Ig	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:08
104	1	(angiogen\$ ADJ factor) same fusion same Immunoglobulin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:09
110	0	(angiogen\$ ADJ factor) same fusion same icam	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:09
116	2730	vascular ADJ cell ADJ adhesion ADJ molecule or ICAM	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:11
122	7	(angiogen\$ ADJ factor) same (vascular ADJ cell ADJ adhesion ADJ molecule or ICAM)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:12

L Number	Hits	Search Text	DB	Time stamp
1	1637	angiogen\$ ADJ factor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 09:36
7	458339	target\$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 09:36
8	3	(angiogen\$ ADJ factor same target\$).clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 09:38
14	2	(angiogen\$ ADJ factor) same (targeting ADJ molecule) same fusion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 09:53
20	13	(angiogen\$ ADJ factor) same fusion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:08
26	113	vegf ADJ a	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:01
32	122	vegf ADJ c	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:01
38	130	vegf ADJ d	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:01
44	4151	fgf	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:02
50	127	angiopoietin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:02
56	0	(angiogen\$ ADJ factor) same fusion same (vegf ADJ a)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:02
68	0	(angiogen\$ ADJ factor) same fusion same (vegf ADJ d)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:03
74	1	(angiogen\$ ADJ factor) same fusion same (vegf ADJ c)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:03
80	0	(angiogen\$ ADJ factor) same fusion same (vegf ADJ d)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:03
62	1	(angiogen\$ ADJ factor) same fusion same fgf	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/08/14 10:07

intraembryonal mesenchyme. The term of determination is not yet known. The marginal cells of the blood islands differentiate into primordial endothelial cells forming primitive vessels by migration, proliferation, **fusion**, and selection. This "vasculogenesis" is induced by specific matrix components produced by the endothelioblasts themselves and other not known factors. Formation of secondary capillary plexuses is related to organogenesis and takes place by sprouting from preexisting endothelium ("**angiogenesis**"). **Factors** which induce and promote angiogenesis were isolated from different embryonic organs. Migration, proliferation, and tube formation are regulated by extracellular matrix components (fibronectin, laminin). Main features of primordial endothelium of protocapillaries are: irregular profile, abundance of synthetic organelles, lack of plasmalemmal vesicles and basement membrane, production of specific matrix components. Specialized endothelium (continuous, fenestrated, discontinuous a.s.o.) develops from secondary plexuses influenced by factors of the specific organ tissue. The probably mechanism by which the endotheliocytes reach their final shape and behavior is discussed; some morphological and functional properties during maturation are documented. The maturation of endothelium is related to establishing of the specific blood-tissue barrier.

=> D HIS

(FILE 'HOME' ENTERED AT 10:54:01 ON 14 AUG 2002)

FILE 'MEDLINE' ENTERED AT 10:54:13 ON 14 AUG 2002

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L1          5 S VEGF FUSION PROTEIN
L2          2539 S ANGIOGEN? FACTOR
L3          99306 S FUSION
L4          208235 S TARGET?
L5           5 S L2 (S) L3 (S) L4
L6          5634 S VASCULAR ENDOTHELIUM
L7          373 S L4 (S) L6
L8           1 S L4 (S) L6 (S) L2
L9           1 S L3 (S) L6 (S) L2
L10         13 S L2 (S) L3
L11         8803 S ICAM OR VCAM
L12        12179 S VASCULAR CELL ADHESION MOLECULE OR INTERCELLULAR ADHESION MOL
L13           0 S L12 (S) L2 (S) FUSION
L14           0 S L12 (L) L2 (L) FUSION
L15           1 S L12 (L) VEGF? (L) FUSION
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FILE 'PCTFULL, USPATFULL, CAPLUS, MEDLINE, BIOSIS, EMBASE, CONFSCI'
ENTERED AT 11:19:20 ON 14 AUG 2002

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L16           3 S L8
L17           2 S L9
L18          78 S L10
L19        130196 S FUSION PROTEIN
L20          44 S L2 (S) L19
L21           1 S L13
L22          161 S L14
L23          140 S L2 (L) L12 (L) L19
L24           1 S L2 (S) L12 (S) L19
L25           5 DUP REM L16 L17 L21 L24 (2 DUPLICATES REMOVED)
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=> D L20 1-44 IBIB ABS

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L20    ANSWER 1 OF 44    PCTFULL    COPYRIGHT 2002 Univentio
ACCESSION NUMBER:      2002059377 PCTFULL ED 20020809 EW 200231
TITLE (ENGLISH):       METHODS OF DIAGNOSIS OF BREAST CANCER, COMPOSITIONS AND
                        METHODS OF SCREENING FOR MODULATORS OF BREAST CANCER
TITLE (FRENCH):        PROCEDES DE DIAGNOSTIC DU CANCER DU SEIN, COMPOSITIONS
                        ET PROCEDES DE CRIBLAGE DE MODULATEURS DU CANCER DU
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transfection rates, were directly assayed for the biological and/or targeting activity of the excreted **fusion proteins** without any prior purification steps. This procedure might help to identify those **fusion proteins** that have favourable characteristics like stability and biological activity in the presence of serum and at low protein concentrations. Targeted delivery of all effector principles was subsequently assessed in an in vitro model system. The method we devised is both rapid and versatile and can be useful to construct and identify series of new chimeric proteins with enhanced therapeutic potential in human cancer therapy.

L20 ANSWER 35 OF 44 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:109274 BIOSIS

DOCUMENT NUMBER: PREV199900109274

TITLE: Vascular endothelial growth factor chimeric toxin is highly active against endothelial cells.

AUTHOR(S): Arora, Naveen; Masood, Rizwan; Zheng, Tong; Cai, Jie; Smith, D. Lynne; Gill, Parkash S. (1)

CORPORATE SOURCE: (1) Norris Cancer Hosp. Res. Inst., Room 3438, 1441 Eastlake Ave., Los Angeles, CA 90033 USA

SOURCE: Cancer Research, (Jan. 1, 1999) Vol. 59, No. 1, pp. 183-188.

ISSN: 0008-5472.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Angiogenesis is a critical step in a benign tumor's evolution toward malignancy and metastasis. Tumor cells acquire such a phenotype by their ability to secrete **angiogenic factors** such as vascular endothelial growth factor (VEGF). VEGF receptors (VEGFRs) flt-1/VEGFR-1 and Flk-1/KDR/EGFR-2 are restricted to activated endothelial cells, with the highest expression being in the tumor vasculature. The present study was undertaken to target the VEGFRs. Targeted toxins were developed by recombinant methods by fusing VEGF165 or VEGF121 to the diphtheria toxin (DT) translocation and enzymatic domain (DT390-VEGF165 or DT390-VEGF121). Both **fusion proteins** were found to be highly toxic to proliferating endothelial cells but not to vascular smooth muscle cells. The **fusion protein** is also active in Kaposi's sarcoma, a tumor type that expresses high levels of VEGFRs. These **fusion proteins** completely inhibit the basic fibroblast growth factor-induced growth of new blood vessels in the chick chorioallantoic membrane assay. Furthermore, the fusion toxin substantially retards the growth of Kaposi's sarcoma tumors in mice. Because nearly all tumors induce local angiogenesis with high VEGFR expression, VEGF-derived toxins may have wide application in cancer therapy.

L20 ANSWER 36 OF 44 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:83075 BIOSIS

DOCUMENT NUMBER: PREV199800083075

TITLE: PlGF-saporin fusion protein: A potential anti-angiogenic agent.

AUTHOR(S): Chiaramonte, R. (1); Polizzi, D.; Bartolini, E.; Petroni, D.; Comi, P.

CORPORATE SOURCE: (1) Dep. Biomedical Sci. Technologies, Univ. Milan, LITA, via Fratelli Cervi 93, Segrate, Milan Italy

SOURCE: Anti-Cancer Drug Design, (Dec., 1997) Vol. 12, No. 8, pp. 649-657.

ISSN: 0266-9536.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Vascularization is an important step in tumor growth and metastasis. Tumor neovascularization can be considered, therefore, as a good target for antineoplastic therapy. In order to target saporin, a powerful plant toxin, in proximity of the tumor we fused the saporin coding sequence to that for placental growth factor-2 (PlGF-2). PlGF is an **angiogenic**

induction of apoptosis. The therapeutic effect may be achieved by direct administration of the chimeric polypeptide, or by transfecting cells with a vector including a nucleic acid encoding such a chimeric polypeptide.

L20 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:816742 CAPLUS

DOCUMENT NUMBER: 135:353711

TITLE: **Fusion proteins of angiogenic factors** and cell adhesion molecules for therapeutic control of angiogenesis

INVENTOR(S): Jiang, Wen G.

PATENT ASSIGNEE(S): University of Wales College of Medicine, UK

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083562	A2	20011108	WO 2001-GB1956	20010504
WO 2001083562	A3	20020131		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001056464	A5	20011112	AU 2001-56464	20010504
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PRIORITY APPLN. INFO.: GB 2000-10630 A 20000504

WO 2001-GB1956 W 20010504

AB Proteins that can antagonize angiogenic factors and that can be used for the therapeutic regulation of angiogenesis, e.g. in the treatment of cancer, and synthetic genes encoding them are described. The proteins include sequences from angiogenic factors and proteins regulating vascular endothelium structure. The angiogenic factors may include vascular endothelial growth factor, basic fibroblast growth factors, scatter factor or chemokines. The protein regulating the vascular endothelial structure may be a cadherin, selectin, or other cell adhesion mol. Also described are methods for prepg. the recombinant polynucleotide, proteins encoded by such polynucleotides and their use in gene or protein therapy for the treatment of conditions such as cancer.

L20 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:781077 CAPLUS

DOCUMENT NUMBER: 135:348849

TITLE: **Albumin fusion proteins with therapeutic proteins for improved shelf-life**

INVENTOR(S): Rosen, Craig A.; Haseltine, William A.

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA

SOURCE: PCT Int. Appl., 413 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079442	A2	20011025	WO 2001-US11850	20010412

induction of apoptosis. The therapeutic effect may be achieved by direct administration of the chimeric polypeptide, or by transfecting cells with a vector including a nucleic acid encoding such a chimeric polypeptide.

L20 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:148753 CAPLUS

DOCUMENT NUMBER: 136:211870

TITLE: Production of biologically active epidermal growth factor fusion proteins with human fibronectin collagen binding domain, retaining high collagen affinity

INVENTOR(S): Ishikawa, Tetsuya; Kitajima, Takashi

PATENT ASSIGNEE(S): Terumo Corp., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 33 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060400	A2	20020226	JP 2000-247379	20000817

AB This invention provides biol. active fusion proteins of an angiogenic regulatory factor with human fibronectin collagen binding domain (FNCBD, 260-599 fragment of fibronectin). FNCBD is obtained by proteolytic degrdn. of FN. Angiogenic factors such as PDGF super family growth factors, VEGF121 and VEGF165 are used. Recombinant expression of the fusion proteins in bacteria and use as biomaterial or sustained-release prepn. and other forms of drug delivery system, are claimed. Both fusion protein FNCBD-VEGF121 and FNCBD-VEGF165 expressed in E. coli were able to bind to collagen and the binding of these proteins with collagen could stimulate proliferation of microvessel endothelial cells (epithelial cells). The collagen-binding hybrid polypeptide can be used as carrier for sustained release of functional peptide in drug delivery system.

L20 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:936090 CAPLUS

DOCUMENT NUMBER: 136:58776

TITLE: Chimeric polypeptides of serum albumin and uses related thereto

INVENTOR(S): Gyuris, Jenő; Lamphere, Lou

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 619,285.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001056075	A1	20011227	US 2001-764918	20010118
US 2002048571	A1	20020425	US 2001-768183	20010123

PRIORITY APPLN. INFO.: US 1999-144534P P 19990719

US 2000-619285 A2 20000719

US 2001-764918 A2 20010118

AB The present invention relates to chimeric polypeptides in which a serum albumin protein has been altered to include one or more biol. active heterologous peptide sequences. The chimeric polypeptides may exhibit therapeutic activity related to the heterologous peptide sequences coupled with the improved serum half-lives derived from the serum albumin protein fragments. Heterologous peptide sequences may be chosen to promote any biol. effect, including angiogenesis inhibition, antitumor activity, and